PROFESSIONAL INFORMATION FOR

IBUGESIC ORAL SUSPENSION

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

IBUGESIC ORAL SUSPENSION (oral suspension)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 mL contains 100 mg of ibuprofen.

Preservatives:	Sodium methyl parahydroxybenzoate 0,172 % *m/v*
	Sodium propyl parahydroxybenzoate 0,045 % *m/v*
	Sodium benzoate 0,1 % *m/v*
Contains sugar:	Maltitol 1,375 g/5 mL.
Contains sweetener:	Saccharin sodium 15 mg/5 mL.

For the full list of excipients, see **section 6.1**.

3. PHARMACEUTICAL FORM

Oral suspension.

Off-white coloured suspension with a characteristic strawberry flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

IBUGESIC ORAL SUSPENSION is indicated for treatment of:

- mild to moderate pain of inflammatory origin for a maximum treatment period of 10 days.
- fever of inflammatory origin.
- post-traumatic conditions.
- the emergency treatment of acute attacks of gout for a maximum treatment period of 5 days.

4.2 Posology and method of administration

Posology

USE THE LOWEST EFFECTIVE DOSE FOR THE SHORTEST POSSIBLE DURATION OF TREATMENT.

Adults:

The recommended dosage of IBUGESIC ORAL SUSPENSION is 600 mg 6 to 8 hourly.

The total daily dose of IBUGESIC ORAL SUSPENSION should not exceed 1,200 mg.

Special populations

Elderly:

The elderly are at increased risk of serious consequences of adverse reactions. If **I**BUGESIC ORAL SUSPENSION is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for gastrointestinal bleeding during therapy. If renal or hepatic function is impaired, the dosage should be assessed individually.

Paediatric population

Children:

The total daily dosage of IBUGESIC ORAL SUSPENSION is 20 mg/kg (1 mL/kg) of body mass given in divided doses.

Safety in children under 1 year has not been proven (see **section 4.3**).

Pain:

Initial dose 5 mg/kg (0,25 mL/kg) of body weight. A second dose of 5 mg/kg may be given after 2 hours if pain is not controlled. Thereafter, 5 mg/kg every 4 to 6 hours.

DO NOT EXCEED 20 mg/kg of bodyweight per day. If pain persists for more than 7 days, a medical practitioner should be consulted.

Fever:

Administer 5 mg/kg of bodyweight every 4 to 6 hours.

DO NOT EXCEED 20 mg/kg of bodyweight per day.

If fever persists for more than 3 days, a medical professional should be consulted.

Dosage for suspension:

Age	***Bodyweight***	***Daily dosage***
1 to 2 years	7 to 12 kg	2,5 mL up to 3 to 4 times daily
3 to 7 years	14 to 23 kg	2,5 to 5 mL up to 3 to 4 times daily
8 to 12 years	25 to 40 kg	10 mL up to 3 to 4 times daily

Children weighing less than 7 kg or younger than 1 year of age should not be given IBUGESIC ORAL SUSPENSION.

Method of administration

IBUGESIC ORAL SUSPENSION is for oral administration. It should preferably be taken with or after food.

4.3 Contraindications

IBUGESIC ORAL SUSPENSION is contraindicated in:

- patients with known hypersensitivity to ibuprofen or to any of the excipients in IBUGESIC ORAL SUSPENSION (see **section 6.1**).
- patients with heart failure.
- patients with a history of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous use of NSAIDs.
- patients with active or a history of recurrent peptic ulcers/haemorrhages/perforations.
- patients sensitive to aspirin or other non-steroidal anti-inflammatory medicines (NSAIDs) or patients with a history of severe allergic reactions, such as anaphylaxis or angioedema, induced by aspirin or other NSAIDs, because of the possibility of cross-sensitivity due to structural relationships which exist among non-steroidal anti-inflammatory medicines. Acute allergic reactions are likely to occur in patients who have exhibited allergic reactions to these medicines.
- lithium, as risk of toxicity is increased.
- patients with aspirin-induced nasal polyps associated with bronchospasm.
- children under the age of 1 year.
- pregnancy and lactation (see **section 4.6**).
- patients with conditions involving a tendency to bleeding.
- patients with severe hepatic failure or renal failure.

4.4 Special warnings and precautions for use

The antipyretic, analgesic and anti-inflammatory action of IBUGESIC ORAL SUSPENSION may mask symptoms or the presence or worsening of infections.

Caution is required in patients with a history of hypertension as fluid retention and oedema have been reported in association with IBUGESIC ORAL SUSPENSION therapy (see **section 4.3** and **section 4.8**).
In view of IBUGESIC ORAL SUSPENSION's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.

The elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal perforation, ulceration and bleeding (PUBs), which may be fatal. The risk of gastrointestinal bleeding or perforation is higher with increasing doses of IBUGESIC ORAL SUSPENSION, in patients with a history of ulcers, and in the elderly. When gastrointestinal bleeding or ulceration occurs in patients receiving IBUGESIC ORAL SUSPENSION, treatment with IBUGESIC ORAL SUSPENSION should be stopped.

Patients with a history of gastrointestinal disease, particularly the elderly, should report any unusual abdominal symptoms (especially gastrointestinal bleeding), particularly in the initial stages of treatment.

Other side-effects include nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease, and gastritis (see **section 4.8**).

IBUGESIC ORAL SUSPENSION should be given with caution to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, gastro-oesophageal reflux disease, angiodysplasia) as these conditions may be exacerbated (see **section 4.8**).

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. IBUGESIC ORAL SUSPENSION should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity (see **section 4.8**).

IBUGESIC ORAL SUSPENSION should be given with care to the elderly, to patients with asthma or bronchospasm and cardiovascular disease (see **section 4.3**).

Patients with cirrhosis, diuretic-induced volume depletion, or renal insufficiency require local synthesis of vasodilating prostaglandins to maintain renal perfusion, and therefore these patients are at greater risk of developing renal dysfunction due to NSAID-induced inhibition of renal prostaglandin synthesis.

IBUGESIC ORAL SUSPENSION should be discontinued in patients who experience blurred or diminished vision, or changes in colour vision (see **section 4.8**).

Patients with collagen disease, including systemic lupus erythematosus, may be at risk of developing aseptic meningitis (see below).

IBUGESIC ORAL SUSPENSION should be given with caution to patients with anaemia.

IBUGESIC ORAL SUSPENSION should be given with caution to patients with stomatitis.

Caution should be advised in patients receiving concomitant medicines which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin reuptake inhibitors or antiplatelet agents, such as aspirin (see **section 4.5**).

Long-term administration of IBUGESIC ORAL SUSPENSION has resulted in renal papillary necrosis and other renal pathologic changes. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of a NSAID, such as IBUGESIC ORAL SUSPENSION, may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors and the elderly. Discontinuation of IBUGESIC ORAL SUSPENSION therapy is usually followed by recovery to the pre-treatment state.

Risk of renal tubular acidosis and hypokalaemia are associated with non-steroidal anti-inflammatory medicine (NSAID) usage.

IBUGESIC ORAL SUSPENSION can interfere with platelet aggregation and has been shown to prolong bleeding time in normal subjects.

Aseptic meningitis has been observed on rare occasions in patients on ibuprofen, as in IBUGESIC ORAL SUSPENSION, therapy. Although it is probably more likely to occur in patients with

systemic lupus erythematosus and related connective tissue diseases, it has been reported in patients who do not have an underlying chronic disease. IBUGESIC ORAL SUSPENSION is contraindicated in pregnancy and lactation (see **section 4.3**).

Maltitol

IBUGESIC ORAL SUSPENSION contains maltitol and may have a laxative effect. Patients with the rare hereditary condition of maltitol intolerance should not take IBUGESIC ORAL SUSPENSION.

4.5 Interaction with other medicines and other forms of interaction

Corticosteroids

There is an increased risk of gastrointestinal perforation, ulceration and bleeding (PUBs) when IBUGESIC ORAL SUSPENSION is co-administered with corticosteroids.

Anticoagulants

Co-administration of IBUGESIC ORAL SUSPENSION with anticoagulants may enhance the effects of anticoagulants, such as warfarin, and increase the possibility of gastrointestinal ulceration or bleeding.

Antiplatelet agents (clopidogrel, ticlopidine)

There is an increased risk of gastrointestinal bleeding if IBUGESIC ORAL SUSPENSION is co-administered with these medicines.

Selective serotonin reuptake inhibitors (SSRIs)

There is an increased risk of gastrointestinal bleeding if IBUGESIC ORAL SUSPENSION is co-administered with these medicines.

Alcohol, bisphosphonates, pentoxifylline

Concomitant administration with IBUGESIC ORAL SUSPENSION poses an increased risk of gastrointestinal ulceration and bleeding (PUBs).

Antidiabetic medicines

The hypoglycaemic effects of these medicines may be increased.

Digoxin

Co-administration with IBUGESIC ORAL SUSPENSION may cause an increase in serum digoxin concentrations. NSAIDs, such as IBUGESIC ORAL SUSPENSION, may also exacerbate cardiac failure and reduce glomerular filtration rate in patients taking digoxin.

Lithium

Lithium and IBUGESIC ORAL SUSPENSION co-administration may increase the steady-state concentration of lithium.

Methotrexate

Increased and prolonged methotrexate plasma concentration and an increased risk of methotrexate toxicity may occur when methotrexate and IBUGESIC ORAL SUSPENSION are given concomitantly.

Nephrotoxic medicines, e.g. ciclosporin

There is an increased risk of nephrotoxicity when nephrotoxic medicines are co-administered with IBUGESIC ORAL SUSPENSION. There is also a possible increased risk of nephrotoxicity when IBUGESIC ORAL SUSPENSION is given with tacrolimus.

Antihypertensive or diuretic medicines

Reduction or reversal of the antihypertensive effect may occur. Diuretics can also increase the risk of nephrotoxicity of NSAIDs, including that of IBUGESIC ORAL SUSPENSION.

Bone marrow depressants

The leukopenic and/or thrombocytopenic effects of these medicines may be increased.

Non-steroidal anti-inflammatory medicines (NSAIDs)

Use of two or more NSAIDs, including cyclo-oxygenase-2 inhibitors, concomitantly could result in an increase in side effects. Concomitant administration of IBUGESIC ORAL SUSPENSION and aspirin is not recommended because of the potential of increased adverse effects (see **section 4.4**).

Quinolone antibiotics

Patients taking NSAIDs, such as IBUGESIC ORAL SUSPENSION, and quinolones may have an increased risk of developing convulsions.

Zidovudine

There is an increased risk of haematological toxicity when NSAIDs, such as IBUGESIC ORAL SUSPENSION, are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in Human Immunodeficiency Virus positive [HIV(+)]

haemophiliacs receiving concomitant treatment with zidovudine and IBUGESIC ORAL SUSPENSION.

Aminoglycosides

NSAIDs, such as IBUGESIC ORAL SUSPENSION, may decrease the excretion of aminoglycosides.

Herbal extracts

Ginkgo biloba may potentiate the risk of bleeding with NSAIDs, such as IBUGESIC ORAL SUSPENSION.

CYP2C9 inhibitors

Concomitant administration of IBUGESIC ORAL SUSPENSION and CYP2C9 inhibitors may increase the exposure to ibuprofen (CYP2C9 substrate). In a study with voriconazole and fluconazole (CYP2C9 inhibitors), an increased S (+)-ibuprofen exposure by approximately 80 to 100 % has been shown. Reduction of the IBUGESIC ORAL SUSPENSION dose should be considered when potent CYP2C9 inhibitors are administered concomitantly, particularly when high-dose ibuprofen is administered with either voriconazole or fluconazole.

4.6 Fertility, pregnancy and lactation

Pregnancy

IBUGESIC ORAL SUSPENSION is contraindicated during pregnancy (see **section 4.3**).

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of

cardiac malformation and gastroschisis after the use of a prostaglandin synthesis inhibitor, such as IBUGESIC ORAL SUSPENSION, in early pregnancy. In animals, the administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation losses, and embryo/foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

Use of non-steroidal anti-inflammatory medicines, such as IBUGESIC ORAL SUSPENSION, during the third trimester of pregnancy may result in premature closure of the foetal ductus arteriosus *in utero* and possibly in persistent pulmonary hypertension of the newborn. The onset of labour may be delayed and its duration increased (see **section 4.3**).

In addition, use of NSAIDs, such as IBUGESIC ORAL SUSPENSION**,** around 20 weeks gestation or later in pregnancy may cause a rare but serious foetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment.
Complications of prolonged oligohydramnios include limb contractures and delayed lung maturation, which may require invasive procedures such as exchange transfusion or dialysis, in some cases.

At the end of pregnancy, prostaglandin synthesis inhibitors, such as IBUGESIC ORAL SUSPENSION, may expose the mother and the neonate to possible prolongation of bleeding time.

Breastfeeding

IBUGESIC ORAL SUSPENSION, appears in breast milk. IBUGESIC ORAL SUSPENSION is contraindicated during lactation (see **section 4.3**).

Fertility

If IBUGESIC ORAL SUSPENSION is used by a woman attempting to conceive, the dose should be kept as low and duration of treatment as short as possible.

4.7 Effects on ability to drive and use machines

Undesirable effects, such as dizziness, drowsiness, fatigue and visual disturbances, are possible after taking IBUGESIC ORAL SUSPENSION. Patients should be advised not to drive or operate machinery until they know how IBUGESIC ORAL SUSPENSION affects them.

4.8 Undesirable effects

Tabulated summary of adverse reactions

MedDRA system organ class	**Frequency**	**Side effects**
Infections and infestations	Less frequent	Rhinitis and aseptic meningitis (see **section 4.4**).
Blood and lymphatic system disorders:	Frequent	Agranulocytosis, thrombocytopenia, anaemia, neutropenia, eosinophilia.
	Less frequent	Leukopenia, aplastic anaemia, haemolytic anaemia.
Immune system disorders	Frequent	Hypersensitivity reactions (fever, rashes, hepatotoxicity, aseptic meningitis).
	Frequency unknown	Non-specific allergic reaction and anaphylaxis, respiratory tract reactivity (comprising asthma, aggravated asthma, bronchospasm, or dyspnoea), assorted skin disorders (pruritus, urticaria, purpura, angioedema, exfoliative and bullous dermatoses – also see Skin and subcutaneous tissue disorders below).
Metabolism and nutrition disorders	Frequency unknown	Hypokalaemia (see **section 4.4**).
Psychiatric disorders	Frequent	Nervousness, depression, insomnia.
	Less frequent	Anxiety, confusional state, hallucinations.

Nervous system disorders	Frequent	Dizziness, drowsiness, headache.
	Less frequent	Paraesthesia, somnolence.
Eye disorders	Frequent	Blurred vision, changes in visual colour perception and other toxic amblyopia.
	Less frequent	Optic neuritis, visual impairment, toxic optic neuropathy.
Ear and labyrinth disorders	Frequent	Tinnitus.
	Less frequent	Impaired hearing, vertigo.
Cardiac disorders	Frequent	Tachycardia, oedema.
	Frequency unknown	Cardiac failure, hypertension (see **section 4.4**).
Vascular disorders	Frequent	Flushing and increase in blood pressure.
Gastrointestinal disorders	Frequent	Abdominal discomfort, peptic ulceration, gastrointestinal bleeding, nausea, vomiting, abdominal cramps and pain, diarrhoea, flatulence, constipation, dyspepsia, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see **section 4.4**).
	Less frequent	Gastritis, gastrointestinal perforation, pancreatitis.

	Frequency unknown	Transient burning in the mouth or throat.
Hepatobiliary disorders	Frequent	Hepatitis.
	Less frequent	Abnormalities in liver function, hepatic failure, jaundice.
Skin and subcutaneous tissue disorders	Frequent	Allergic dermatitis, erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis (see Immune system disorders).
	Less frequent	Photosensitivity reaction.
Renal and urinary disorders	Frequent	Impairment of renal function, acute reversible renal impairment, intestinal nephritis and nephrotic syndrome.
	Less frequent	Renal failure.
	Frequency unknown	Renal tubular acidosis (RTA) (see **section 4.4**).
General disorders	Less frequent	Malaise, fatigue.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reactions Reporting Form”, found online under SAHPRA’s publications:

https://www.sahpra.org.za/Publications/Index/8 or to Cipla Medpro (Pty) Ltd. by email: drugsafetysa@cipla.com or telephone: 080 222 6662 (toll free).

4.9 Overdose

Symptoms:

Most patients who have ingested significant amounts of ibuprofen, as in IBUGESIC ORAL SUSPENSION, will manifest symptoms within 4 to 6 hours.

The most frequently reported symptoms of overdose include nausea, vomiting, abdominal pain, lethargy and drowsiness. Central nervous system (CNS) effects include headache, tinnitus, dizziness, convulsion and loss of consciousness. Nystagmus, metabolic acidosis, hypothermia, renal effects, gastrointestinal bleeding, coma, apnoea, diarrhoea and depression of the central nervous and respiratory systems have also less frequently been reported. Disorientation, excitation, fainting and cardiovascular toxicity, including hypotension, bradycardia and tachycardia have been reported. In cases of significant overdose, renal failure and liver damage are possible.

Therapeutic measures:

Patients should be treated symptomatically as required. Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered.

Good urine output should be ensured. Renal and liver function should be closely monitored. Patients should be observed for at least four hours after ingestion of potentially toxic amounts. Frequent or prolonged convulsions should be treated with intravenous diazepam. Other measures may be indicated by the patient’s clinical condition. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.3.1. Antirheumatics (anti-inflammatory agents)

ATC code: M01AE01

Ibuprofen is a propionic acid derivative with analgesic, anti-inflammatory and antipyretic activity. Ibuprofen's therapeutic effects as a non-steroidal anti-inflammatory drug (NSAID) are thought to result from its inhibitory effect on the enzyme cyclo-oxygenase, which results in a marked reduction in prostaglandin synthesis.

5.2 Pharmacokinetic properties

Ibuprofen is well absorbed after oral administration. The onset of action for pain relief is 30 minutes and the time for peak effect for fever is 2 to 4 hours. The half-life of ibuprofen is about 2 hours. More than 90 % of an ingested dose is excreted in the urine as metabolites or their conjugates.

Ibuprofen inhibits platelets aggregation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- carboxymethylcellulose sodium.
- citric acid monohydrate.
- liquid maltitol.
- microcrystalline cellulose.
- polysorbate 80.
- saccharin sodium.
- sodium benzoate.

- sodium citrate dihydrate.
- sodium methyl parahydroxybenzoate.
- sodium propyl parahydroxybenzoate.
- strawberry flavour.
- xanthan gum.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

- Store at or below 25 °C.
- Protect from light. Shake well before use.
- Keep well closed. Do not refrigerate.

6.5 Nature and contents of container

IBUGESIC ORAL SUSPENSION is packed in 100 mL amber coloured transparent PET bottle with a pilfer-proof, child-resistant cap. The amber PET bottle that is closed with CR caps is then placed in carton with leaflets and 5 mL syringe.

Pack sizes: 100 mL.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

CIPLA MEDPRO (PTY) LTD.

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Mispel Street

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8. REGISTRATION NUMBER(S)

37/3.1/0468

Botswana:	S3 BOT1702929

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First authorisation: 03 June 2005.

Latest renewal: Not applicable.

10. DATE OF REVISION OF THE TEXT

12 July 2024